

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year)

03 December 1996 (03.12.96)

International application No.

PCT/EP96/01706

Applicant's or agent's file reference

PT/PJS/P31158

International filing date (day/month/year)

23 April 1996 (23.04.96)

Priority date (day/month/year)

24 April 1995 (24.04.95)

Applicant

VERE HODGE, Richard, Anthony et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

11 November 1996 (11.11.96)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

A. Addae-Ruesch

Telephone No.: (41-22) 730.91.11

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PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PTPJS/P31158	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 96/01706	International filing date (day/month/year) 23/04/96	(Earliest) Priority Date (day/month/year) 24/04/95
Applicant SMITHKLINE BEECHAM P.L.C. et al.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☒ Certain claims were found unsearchable (see Box I).

2. ☐ Unity of invention is lacking (see Box II).

3. ☐ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing

☐ filed with the international application.

☐ furnished by the applicant separately from the international application,

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority

4. With regard to the title, ☐ the text is approved as submitted by the applicant

☒ the text has been established by this Authority to read as follows:

USE OF (R)-PENCICLOVIR TRIPHOSPHATE FOR THE MANUFACTURE OF A MEDICAMENT FOR THE TREATMENT OF VIRAL DISEASES

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is:

Figure No. ☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 96/01706

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 4-7
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
The terms "bioprecursor" and "derivative" do not precisely define a compound.

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

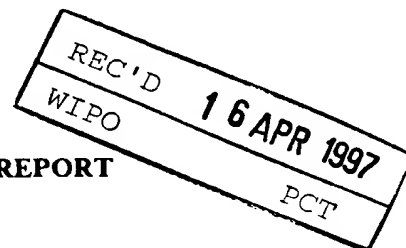
- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

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PATENT COOPERATION TREATY
PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)




Applicant's or agent's file reference PT/P31158	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP 96/ 01706	International filing date (day/month/year) 23/04/1996	Priority date (day/month/year) 24/04/1995
International Patent Classification (IPC) or national classification and IPC A61K31/52		
Applicant SMITHKLINE BEECHAM P.L.C. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This **REPORT** consists of a total of 6 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consists of a total of _____ sheets.

3. This report contains indications and corresponding pages relating to the following items:
- I ☒ Basis of the report
 - II ☐ Priority
 - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☒ Certain observations on the international application

Date of submission of the demand 11/11/1996	Date of completion of this report 14.04.97
Name and mailing address of the IPEA/  European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer <i>D. Tzschoppe</i> D.A. TZSCHOPPE Telephone No.

I. Basis of the report

1. This report has been drawn up on the basis of (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

☒ the international application as originally filed.

☐ the description, pages _____, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☐ the claims, Nos. _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. _____, filed with the letter of _____,
Nos. _____, filed with the letter of _____.

☐ the drawings, sheets/fig _____, as originally filed,
sheets/fig _____, filed with the demand;
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____.
☐ the claims, Nos. _____.
☐ the drawings, sheets/fig _____.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 7 _____

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international preliminary examination (specify):

☒ the description, claims or drawings (indicate particular elements below) or said claims Nos. 7 _____ are so unclear that no meaningful opinion could be formed (specify):

The term "derivative" does not clearly define a chemical compound

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Intern. application No.
PCT/EP96/01706

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1, 2	YES
	Claims 3-6	NO
Inventive Step (IS)	Claims	YES
	Claims 1-6	NO
Industrial Applicability (IA)	Claims 3, 5, 6	YES
	Claims 1, 2, 4	NO

2. CITATIONS AND EXPLANATIONS

- 1). The subject-matter of Claims 1 and 2 seems to be novel, since none of the prior art documents cited in the search report describes the claimed use or method.
- 2). The subject-matter of Claims 1 and 2 however does not seem to involve an inventive step for the following reasons:

The effectiveness of penciclovir triphosphate against HIV and HBV infections is already known from D1: WO-A-9200742 (see p.2, line 11 to page 4, line 15 and claims 1-12) and D2: EP-A-388049 (see page 2, line 42 to page 3, line 25 and claims 1-8).

As the skilled man is aware from D3: Antimicrobial Agents and Chemotherapy, vol. 36, no. 12, 1992, pages 2747-2757 (see the abstract; page 2747, left column and page 2751, right column - page 2752, left column) and D4: Antiviral Research & Chemotherapy (see the summary and page 19, right column to page 21, left column) that penciclovir triphosphate exists in form of 2

enantiomers, it is a matter of routine for the skilled man which of the 2 enantiomers is more active in a treatment known for generic penciclovir triphosphate.

- 3). The subject-matter of Claim 3 does not seem to be novel, since a composition comprising (R)-penciclovir triphosphate and which has antiviral activity has already been disclosed by D3 and D4, see at the places indicated above in paragraph 2.
- 4). The subject-matter of Claims 4 to 6 does not seem to be novel, since compounds such as famciclovir or penciclovir, which are bioprecursors of (R)-PCV-TP or (R)-PCV-MP are already known from D1 and D2, see at the places indicated above in paragraph 2.
- 5). The subject-matter of Claims 3, 5 and 6 is considered as having industrial applicability.
- 6). For the assessment of the present Claims 1, 2 and 4 on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but will allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

- 1). Claim 4 is not clear, since it relates to different categories of claims (method, composition or use).
- 2). Claims 4 to 6 are not clear, since the terms "bioprecursor" and "derivative" do not precisely define a chemical compound.

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PTPJS/P31158	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 96/01706	International filing date (day/month/year) 23/04/96	(Earliest) Priority Date (day/month/year) 24/04/95
Applicant SMITHKLINE BEECHAM P.L.C. et al.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.
☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (see Box I).

2. ☐ Unity of invention is lacking (see Box II).

3. ☐ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing

☐ filed with the international application.
☐ furnished by the applicant separately from the international application,
☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority

4. With regard to the title, ☐ the text is approved as submitted by the applicant.
☒ the text has been established by this Authority to read as follows:

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5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.
☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is:

Figure No. _____ ☐ as suggested by the applicant. ☐ None of the figures.

☐ because the applicant failed to suggest a figure.
☐ because this figure better characterizes the invention.

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K31/52 A61K31/66

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	ABSTRACTS OF THE INTERSCIENCE CONFERENCE ON ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, vol. 35, no. 0, 1995, page 191 XP002009432 SU SAN MOK ET AL.: "Preferential inhibition of human hepatitis B virus (HBV) DNA polymerase by the (R)-enantiomer of penciclovir triphosphate" cited in the application see abstract no. H66 --- -/--	1-3



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

26 July 1996

Date of mailing of the international search report

13. 08. 96

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+ 31-70) 340-3016

Authorized officer

Tzschoppe, D

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	ABSTRACTS OF THE INTERSCIENCE CONFERENCE ON ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, vol. 35, no. 0, 1995, page 198 XP002009433 R.F.SCHINAZI ET AL.: "Differential inhibition of viral polymerases by enantiomers of penciclovir triphosphate" see abstract no. H104 ---	1-3
X	ANTIMICROB. AGENTS CHEMOTHER., vol. 36, no. 12, 1992, pages 2747-2757, XP002009434 DAVID L. EARNSHAW ET AL.: "Mode of antiviral action of penciclovir in MRC-5 cells infected with herpes simplex virus type 1 (HSV-1), HSV-2 and varicella-zoster virus"	3-6
Y	see abstract see page 2747, left-hand column see page 2751, right-hand column - page 2752, left-hand column ---	1,2
X	ANTIVIRAL CHEMISTRY & CHEMOTHERAPY, vol. 4, no. supplement 1, 1993, pages 13-24, XP002009435 R.A. VERE HODGE ET AL.: "The mode of action of penciclovir"	3-6
Y	see abstract see page 19, right-hand column - page 21, left-hand column ---	1,2
X	WO,A,92 00742 (BEECHAM GROUP PLC) 23 January 1992	4-6
Y	see page 2, line 11 - page 4, line 15 see claims 1-12 ---	1-3
X	EP,A,0 388 049 (BEECHAM GROUP PLC) 19 September 1990 cited in the application	4-6
Y	see page 2, line 42 - page 3, line 25; claims 1-8 -----	1-3

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 96/01706

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-9200742	23-01-92	AP-A- 291	29-12-93
		AU-B- 647807	31-03-94
		AU-B- 8103291	04-02-92
		CA-A- 2086756	08-01-92
		EP-A- 0538305	28-04-93
		IL-A- 98749	30-03-95

EP-A-388049	19-09-90	AT-T- 122562	15-06-95
		AU-B- 628137	10-09-92
		AU-B- 5060090	01-11-90
		CA-A- 2011238	03-09-90
		DE-D- 69019404	22-06-95
		DE-T- 69019404	12-10-95
		ES-T- 2072386	16-07-95
		HK-A- 116795	21-07-95
		IL-A- 93594	26-05-95
		JP-A- 2275821	09-11-90
